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Ultrasonographic Measures of Volume Responsiveness

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14. ABSTRACT
Ultrasound (US) is a useful tool to manage severely injured soldiers during air transport. The best metric to predict volume responsiveness (VR) is unknown. The most studied measure is respiratory variation in the inferior vena cava, but its accuracy in patients who have had torso surgery is unclear. This was a prospective observational study comparing several US measures in the prediction of VR in critically ill trauma and surgical patients. Over a 3-year period, 202 patients completed the study; 68% were mechanically ventilated and 46% had undergone torso surgery. Respiratory variation in the inferior vena cava was not found to be associated with VR; however, several other metrics including the velocity time integral and respiratory variation in the internal jugular 90° were significantly associated ($p<0.05$). For individual measures, the area under the receiver operating characteristic curve ranged from 0.61-0.71. When the velocity time integral and respiratory variation in the internal jugular 90° were considered together, it rose to 0.78 (confidence interval 0.69-0.85). US can predict VR in ill trauma patients. More sophisticated Doppler measurements appear to be the most accurate. With the development of better software tools and upgrading the ultrasound machines available in transport, US could become an essential part of managing patients' fluid administration during evacuation.

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Ultrasound, volume responsiveness, respiratory variation, focused rapid echocardiographic evaluation, FREE, point-of-care ultrasound, POCUS, cardiac ultrasound

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1.0 SUMMARY

The intended physiologic response to a fluid bolus is an increase in cardiac stroke volume (SV). Several ultrasound (US) measures have been shown to be predicative. The most discussed is respiratory variation in the inferior vena cava (rv IVC), but the majority of studies have been in an older, critically ill medical population. Recently, its accuracy in surgical patients has been challenged. As a result, the best measures in a military population are unclear.

This is a prospective observational study in critically ill surgical and trauma patients receiving a bolus of crystalloid, colloid, or blood. A transthoracic echocardiogram was performed before and after. A positive volume response (+VR) was defined as a ≥15% increase in SV. Predicative measures were left ventricular velocity time integral (VTI), respiratory SV variation (rSVV), passive leg raise SVV, positional internal jugular (IJ) vein change (0-90° IJ), respiratory variation in the IJ sitting upright (90° IJ), and rv IVC. For each measure, the area under the receiver operating characteristic curve (AUROC) was assessed and the best measures determined.

Between November 2013 and November 2015, 202 patients completed the study. The post-bolus VTI could not be interpreted in 3, for a final study group of 199. After the pilot analyses, passive leg raise SVV was abandoned, as it could not be reliably assessed. VTI, rv 90° IJ, and 0-90° IJ were all significantly associated with VR ($p<0.05$); rSVV and rv IVC were not in the group as a whole. For VTI, AUROC was 0.71 (95% confidence interval (CI) 0.64-0.77). For rv 90°**,** it was 0.65 (95% CI 0.57-0.71) and for 0-90° IJ it was 0.61 (95% CI 0.54-0.69). When VTI and rv 90° were considered together, the AUROC rose to 0.76 (95% CI 0.69-0.82) for the population as a whole and 0.78 (CI 0.69-0.85) in mechanically ventilated patients. Respiratory SVV was also predicative in vented patients, with an AUROC of 0.69; rv IVC was not predicative in any subgroup. The positive predicative value for combined assessment was 80% and the negative 70%.

In a relevant heterogeneous trauma population, US is predicative of VR, but it still needs to be refined and developed before widespread military use. These data suggest that upgrading the transport US machines should be considered, as VTI appears to be the most accurate predictor of VR and it can also be used to calculate SV and cardiac output. IJ change and VTI are the best measures of VR, especially when used together. With the development of better software tools and upgrading the US systems, US could become an essential part of managing hemodynamically unstable patients during evacuation.

2.0 INTRODUCTION

Managing a trauma patient who becomes unstable in flight is difficult. A better method of assessing intravascular and cardiac volume status would have a variety of military applications. Ultrasound (US) is portable and non-invasive and allows direct visualization of the heart and great vessels; as such, it is ideal for the management of the combat injured. A limited US system allowing basic two-dimensional (2D) imaging is currently available in flight. The more sophisticated cardiovascular systems for dedicated cardiac imaging (echocardiography) are becoming smaller and more durable. In general, most of the cardiac function assessments, including left ventricular ejection fraction, assessing the respiratory variation, and calculating the stroke volume (SV) and cardiac output using the left ventricular velocity time integral (VTI), are well established and have been used for years by cardiologists. Assessing volume status with US

is relatively new. There are two aspects to volume status: how full the heart is and if it is volume responsive (VR). This study focuses on VR, or how likely the patient is to respond to a fluid bolus with an increase in cardiac SV. The primary intent of this study is to determine 1) if US is predicative of an increase in cardiac SV with a fluid bolus in a trauma population and 2) the best measure or measures in this difficult-to-image population.

3.0 BACKGROUND

Early, aggressive fluid resuscitation in shock is associated with improvement in outcomes including mortality [1]. Multiple studies have supported this concept in a variety of clinical settings, from septic shock to high-risk surgical patients [2-4]. On the other hand, a clear association between cumulative fluid balance and mortality exists [5-7]. It becomes prudent to adopt a tailored approach to fluid resuscitation over empiric fluid loading. In general, a fluid bolus that does not lead to increased SV is unlikely to benefit the patient and carries all of the risks associated with volume overload.

Multiple methods, invasive or otherwise, have been proposed to predict an increase in SV with a fluid bolus, or VR. While central venous pressure (CVP) has traditionally been used to assess volume status, studies have not demonstrated a reliable relationship between CVP and VR [8]. Pulmonary artery catheters have also fallen out of favor at many institutions due to their invasiveness and potential for serious complications [9]. In addition, several studies have failed to show any improvement in outcome associated with pulmonary artery catheter use [10,11]. Given its non-invasive nature, portability, and ease of use as a point-of-care test, US has emerged as an attractive option to assess volume status and predict fluid responsiveness.

The best studied and described US measure to estimate volume status is respiratory variation in the inferior vena cava (rv IVC). This measure is relatively easy to perform with any point-of-care US system [12]. While multiple studies have demonstrated rv IVC accurately predicts VR in mechanically ventilated patients [13-17], there is conflicting evidence in spontaneously breathing patients [18-20]. In many surgical patients, IVC measurement may be difficult, or impossible, to perform secondary to abdominal distension, surgical wounds, morbid obesity, or bowel gas [21,22]. Additionally, evidence suggests that in the setting of increased thoracic or intra-abdominal pressures, IVC diameter and collapsibility indices may lose their reliability [23].

More recently, internal jugular (IJ) vein distensibility has emerged as a parameter for predicting fluid responsiveness, which is also easily assessed with a basic US system. Guarracino et al. demonstrated that IJ vein distensibility is an accurate predictor of VR in mechanically ventilated septic patients [24], while other studies have demonstrated utility using the IJ to detect early hemorrhage in healthy volunteers donating blood [25,26]. Doppler flow assessment, which requires a more advanced machine and more training, can be used to measure respiratory stroke volume variation (rSVV) and may also predict VR [27]. In general, the studies to date are in small populations of medical patients on standard ventilator setting. There are very few studies directly comparing measures, or evaluating the possible additive effect of assessing multiple parameters, and very little is known about the accuracy of these measurements in surgical patients. The primary objective of this study is to directly compare multiple US measures of VR to determine the best measure, or combination of measurements, in critically ill surgical patients.

4.0 METHODS

Adult patients admitted to the intensive care unit (ICU) getting a fluid bolus or blood product transfusion for clinical indications were eligible for enrollment. After informed consent was obtained, patients underwent two transthoracic echocardiograms (TTEs): one immediately prior to the bolus/transfusion (pre-TTE) and a second upon its completion (post-TTE). The SV was assessed in both exams, and the percent change as a result of the fluid was calculated. Patients with an increase ≥15% in the SV were determined to be volume responsive (+VR or -VR). The predicative accuracy of several different US measures in assessing VR were directly compared.

4.1 Enrollment and Data Collection

Over a 36-month period (November 2013 to November 2015), the trauma and surgical ICUs were surveyed Monday-Friday from 7 a.m. to 4 p.m. Patients receiving crystalloid (≥500 cc), colloid (100 cc 25%, or 500 cc 5%), or blood product (≥1 unit of blood, or ≥ 2 units fresh frozen plasma) transfusion were identified. Administration of the fluid was never delayed for either enrollment or performance of the pre-TTE. Clinical data including demographic (age, sex, admission diagnosis) and clinical information (body surface area, mean arterial blood pressure, heart rate, 24-hour fluid balance) were extracted from the medical record. The ventilator settings, and surgeries performed prior to the pre-TTE, were recorded. The type and the amount of the bolus were also noted.

4.2 Echocardiographic Assessment

All exams were performed by a dedicated cardiac sonographer or trained surgical intensivist using a Phillips CX-50 ultrasound system (Andover, MA) with a cardiac calculation package. For the cardiac measurements, a phased array 3S cardiac transducer was used. For the IJ assessment, a high-frequency linear transducer was employed. The pre-TTE was performed within 30 minutes of the fluid administration and the post within 30 minutes of its completion. Both exams were focused rapid echocardiographic exams (FREE) [28,29]. The FREE includes the standard transthoracic four views: parasternal long axis, parasternal short axis, apical (AP), and subxiphiod It is similar to a standard TTE except that the measurements and interpretation are hemodynamically rather than anatomically oriented [28]. Ejection fraction and diastolic function are assessed as part of the FREE. Several predicative measures described below were assessed in the pre-TTE evaluation (Table 1).

4.2.1 Stroke Volume Assessment. In both the pre- and post-TTE, the SV was assessed with pulsed wave Doppler through the left ventricular (LV) outflow tract from the AP window. The VTI was measured, as was the LV outflow tract diameter in the parasternal long axis. These were used to calculate the SV as previously described [28,30]. If the patient was in atrial fibrillation, the average of five beats was taken. If the VTI could not be measured due to anatomic reasons, or aliasing was too high because of high velocity flow, the SV measurements could not be obtained and the patient was excluded from the study. The pre- and post-bolus VTI were recorded and the percent change in SV was determined by the following equation:

$$[(\text{Post-VTI} - \text{Pre-VTI})/\text{Pre-VTI})] * 100$$

Table 1. Ultrasound Measures of Volume Responsiveness

Measure	Description	Assessment	Mode	Difficulty
VTI[a]	Outflow through the aortic valve	Outflow LV	Doppler	+++
0-90° IJ[b]	Positional change in the IJ diameter	Inflow RV	2D	++
rv IJ 90°[c]	Respiratory variation in the IJ at 90°	Inflow RV	2D	+
rv SVV	Variation in SV with respiration	Outflow LV	Doppler	++++
plr SVV	Variation in SV with passive leg raise	Inflow RV/outflow LV	Doppler	++++
rv IVC	Respiratory variation in the IVC	Inflow IVC	2D	++

[a]VTI measures outflow from the LV. It is the central determinant of SV. It requires a machine with a cardiac quality pulsed wave Doppler signal and is moderately difficult to perform.
[b]The 0-90° IJ assesses blood flowing into the right ventricle (RV) by sitting the patient upright and measuring the cross-sectional change. While it can be measured with any system, it requires measuring the IJ in two positions and is mildly difficult to perform.
[c]rv IJ simply involves sitting the patient upright and measuring the maximum and minimum diameter of the IJ at 90°.

4.2.2 Respiratory Variation in the IVC. M-mode: From the sub-costal view, the liver was identified. The IVC was located in long axis passing into the right atrium. A cursor was placed just proximal to the insertion of the hepatic veins, approximately 2 cm into the liver. M-mode was recorded over several respiratory cycles. The maximum and minimum diameters were determined and recorded [15].

4.2.3 Two-Dimensional IVC Assessment. As described above, the IVC was located in long axis. Rather than looking specifically at the hepatic vein insertion, the entire IVC was assessed to determine if there was respiratory variation anywhere along its course. The maximum and minimum measurements were obtained using a caliper. As with the other measurements, the percent change was determined by the difference over the max IVC diameter.

4.2.4 Respiratory SVV. Similar to SV, SVV is obtained from the AP window with pulsed wave Doppler. To determine the rSVV, the sweep speed was decreased to allow visualization of both the maximum and minimum VTI from one screen. If the patient was in atrial fibrillation, the SVV measurements could not be performed. The peak flow and minimum flow were determined and the rSVV was calculated.

$$[(\text{max VTI} - \text{min VTI})/\text{max VTI})]*100$$

4.2.5 Passive Leg Raise SVV. The transducer was placed so the VTI could be measured from the AP window of the heart. For the baseline measurement the patient was flat, with the legs and head of bed flat or at 0°. The baseline tracing was recorded. Then both of the patient's legs were raised 45-90° into the air and the VTI with passive leg raise was recorded. The difference in VTI with passive leg raise was calculated.

4.2.6 Internal Jugular Vein. For this measurement, the transducer was changed to a high-frequency linear (12-MHz) transducer. The left IJ was imaged in short and long axis in the mid neck, first with the patient completely supine (0°) and then with the head of bed upright (90°)

(Figure 1). The patient's head was maintained in a neutral position. The maximal and minimal diameters as a result of respiratory variation were assessed at both positions from the short axis view, as was the change in cross-sectional area as the patient was moved from 0-90°.

Respiratory variation 0°	(rv IJ 0°)	[(IJ 0° max – IJ 0° min)/IJ 0° max] x 100
Respiratory variation 90°	(rv IJ 90°)	[(IJ 90° max – IJ 90° min)/IJ 90° max] x 100
Positional IJ change	(pΔIJ)	[(IJ 0° – IJ 90°)/IJ 0°] x 100

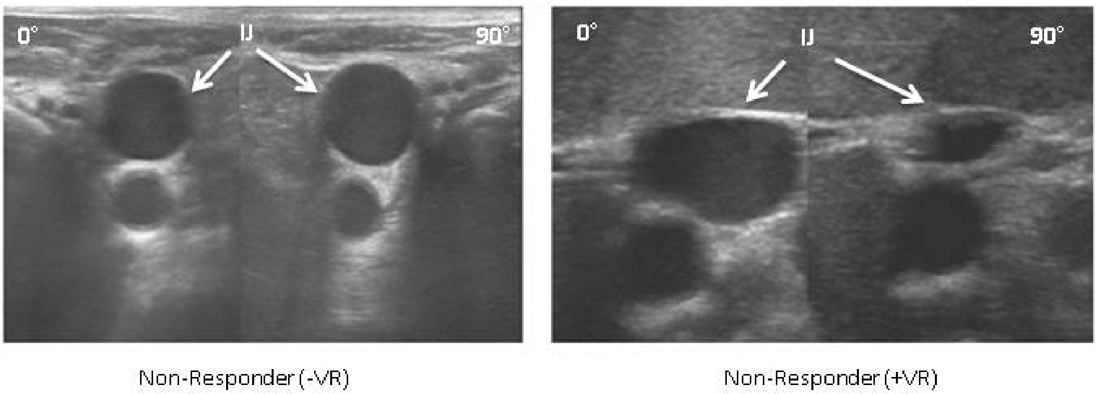

Figure 1. Positional change: IJ vein. *(Left) IJ above the carotid artery with the patient flat (0°) and sitting upright (90°) in a patient who did not respond to a fluid bolus; note that the IJ is unchanged. (Right) Patient whose SV did increase with a fluid bolus; note how the IJ significantly decreased in size with 90° positioning.*

4.3 Data Interpretation and Statistical Analysis

After 50 patients were enrolled, an interim analysis was performed to determine which measures were feasible and to fine tune aspects of how the measurements were being performed. For final analysis, three different reviewers analyzed the US data after collection; all were blinded to the clinical scenario (blood pressure, type of bolus, etc.). The reviewer who analyzed the SV response to fluid was blinded to the predicative measures and vice versa. Two different reviewers both analyzed 25 randomly selected patients, and the inter-observer variability was determined for the predicative measures.

4.4 Statistical Analysis

Patients were separated into two groups: +VR and -VR based on a ≥15% increase in the SV with a fluid bolus. A receiver operating characteristic (ROC) curve was used to determine threshold values for sensitivity and specificity.

Standard ROCs determine a single threshold value that detects the most accurate single measurement. However, US is better understood as a semi-quantitative tool, and thus estimates and ranges are a more accurate way to use the information it provides. There is often a grey area. To create a more useful clinical tool, the criterion and coordinate values of the ROC data were used to create upper and lower threshold values for the best sensitivity and specificity of each measurement (i.e., below X the outcome is very unlikely, above Y it is very likely, between X and Y the value is indeterminate). The number of patients that fell within the grey area was quantified. Logistic regression analysis was used to determine the most predicative combination

of variables. The sensitivity and specificity of each measure were calculated using the threshold values. This allowed comparison of ranges between different measures.

Descriptive statistics were employed using a mean (M) (± standard deviation [SD]) for continuous variables and a number or percentage for categorical variables. A probability of results being due to chance (p-value) of <0.05 was considered statistically significant.

5.0 RESULTS

Over the study period, 242 patients were enrolled; 202 patients completed the study. Three additional patients were removed because the SV could not be determined secondary to aliasing of the VTI waveform, for a final dataset of 199 patients. The most common reasons patients were excluded were inability to image the patient prior to bolus administration or change in the clinical plan. In 11% the SV could not be assessed secondary to anatomic issues (i.e., obesity, subcutaneous air).

5.1 Demographic Data

The average age was 55 (±18 years), 60% were male, and the majority were trauma patients (54%). The average Injury Severity Score was 26±14. Most (68%) were mechanically ventilated at the time of the study, and 46% had undergone thoracic or abdominal surgery prior to the echocardiogram being done (Table 2). The most common type of bolus was crystalloid (64%), followed by blood product (21%) and albumin. The average amount of fluid was 666 (±146 cc).

Table 2. Demographics of Study Group

Demographic	Value
Age, M (±SD)	55 (±18)
Male, % (N)	60 (119)
Body surface area DuBois, M (±SD)	2.00 (±0.25)
Acute care surgery, % (N)	68 (135)
Trauma, % (N)	54 (107)
Injury score (n=71), M (±SD)	26 (±14)
Mechanically ventilated, % (N)	68 (134)
Thoracic/abdominal surgery, % (N)	46 (92)
Other surgery, % (N)	31 (61)
Crystalloid, % (N)	64 (128)
Blood products, % (N)	22 (42)
Albumin, % (N)	14 (28)
Amount of bolus, M (±SD)	666 (±416)
24-h fluid balance, M (±SD)	2794 (±3806)
Length of stay in intensive care unit, M (±SD)	20 (±18)
Length of stay in hospital, M (±SD)	28 (±27)
Mortality, % (N)	19 (37)

5.2 Measurement Data

At the preliminary analysis, it was determined plr SVV could not reliably be measured, and it did not appear to be predicative of +VR. It was very difficult to differentiate SVV secondary to respiration from that resulting from the leg raise. Also, it was very difficult to determine exactly when to measure the waveform after the legs were raised. A significant number of patients had anatomic limitations (i.e., femur or pelvic fractures), and movement of the lower extremities frequently caused the patient some discomfort. This measure was abandoned; all of the other measurements proved feasible and were continued. Upon completion, the IVC was able to be assessed in 78%, the SVV in 87%, and the IJ in 90%.

Thirty-seven percent of patients were +VR and 63% were -VR. Pre-bolus ejection fraction and diastolic function were not associated with VR. Of the measures, only pre-bolus VTI ($p < 0.001$) and IJ measures (rv IJ 0° and pΔIJ; $p<0.001$) were significantly associated with an increase in SV with a fluid bolus.

5.2.1 Pre-Bolus VTI. Pre-bolus VTI, which measures pre-bolus SV, was the single most predicative measure. The area under the ROC (AUROC) was 0.71 (95% confidence interval (CI) 0.64-0.77). Examination of the ROC showed the best threshold values are ≥22 cm to detect non-responders and ≤18 to detect +VR. This allowed assessment in 78% of patients with a sensitivity and specificity of 75% and 70%, respectively (Figure 2).

5.2.2 Internal Jugular Vein. Evaluation of rv IJ 90° was significantly associated with an increase in SV; however, the AUROC was 0.65 (95% CI 0.57-0.71). Positional variation of the IJ also appeared to be a predictor of VR. The AUROC was 0.61 (95% CI 0.54-0.69). When the rv IJ and the VTI were considered together, called combined assessment of volume status (CAVS), the accuracy increased to 0.76 (95% CI 0.69-0.82). Interestingly, when only mechanically ventilated patients were considered, all of the measures were more accurate (Figures 3 and 4).

5.3 Ranges of Variables

By evaluating the ROC criterion, we were able to identify reasonable upper and lower cut-off values for all of the parameters (Table 3). The negative predictive value (NPV) and positive predictive value (PPV) were highest for CAVS, 70 and 80%, respectively, and lowest for rv IVC at 53 and 59%. The single best measure was VTI (74 and 70%, respectively) followed by the IJ assessments with values from 60-70% (Table 3).

5.4 Sub-Group Analysis

5.4.1 Mechanically Ventilated vs. Not Ventilated. The majority of patients were on mechanical ventilation at the time of the study (68%). All of the parameters were more predicative in mechanically ventilated patients. In this group VTI, SVV, and respiratory variation at 90 were all significantly predicative of VR with AUROCs of 0.74, 0.69, and 0.68, respectively. When both VTI and the IJ were considered together with CAVS, the AUROC rose to 0.78 (Figure 4). In non-vented patients, none of the parameters were significantly associated with VR. VTI was the closest, with an AUROC of 0.65 (-0.09-0.05; $p=0.55$).

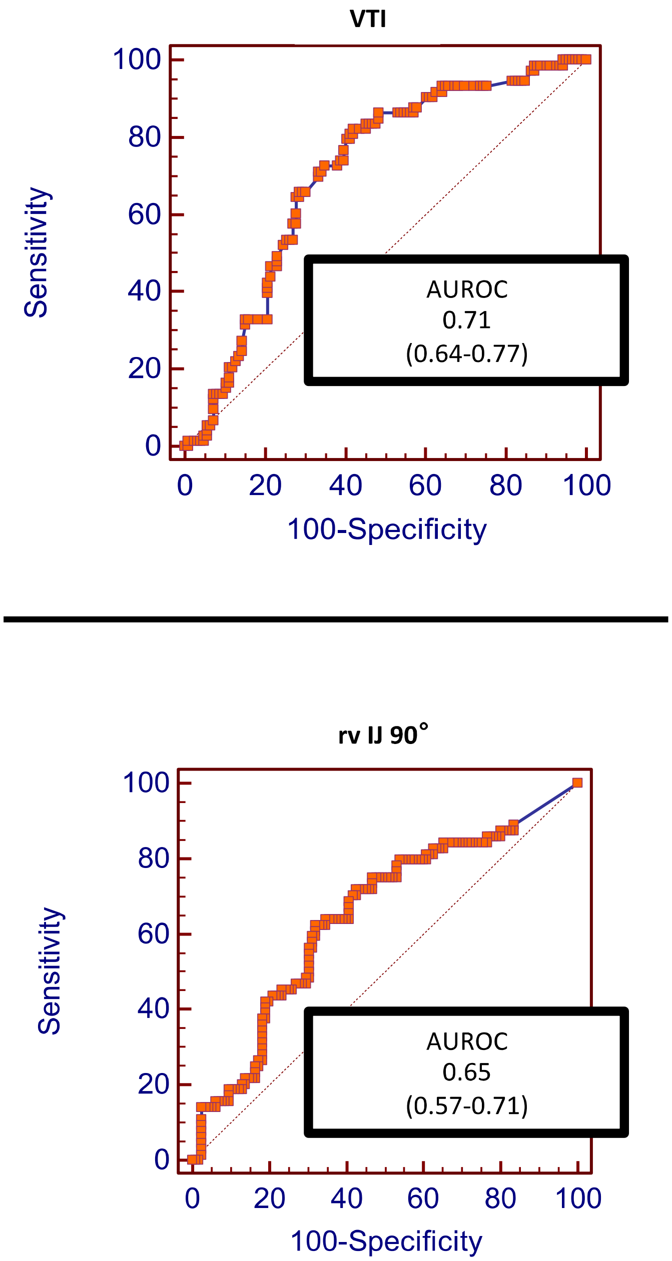

Figure 2. VTI and rv IJ in prediction of VR.

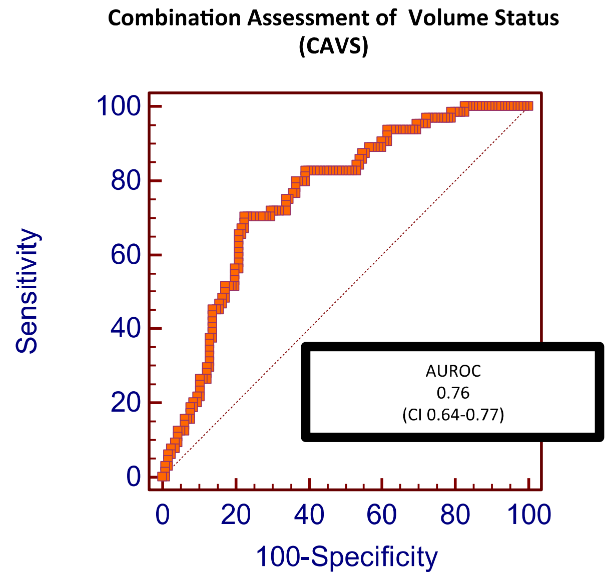

Figure 3. Combination assessment in prediction of VR.

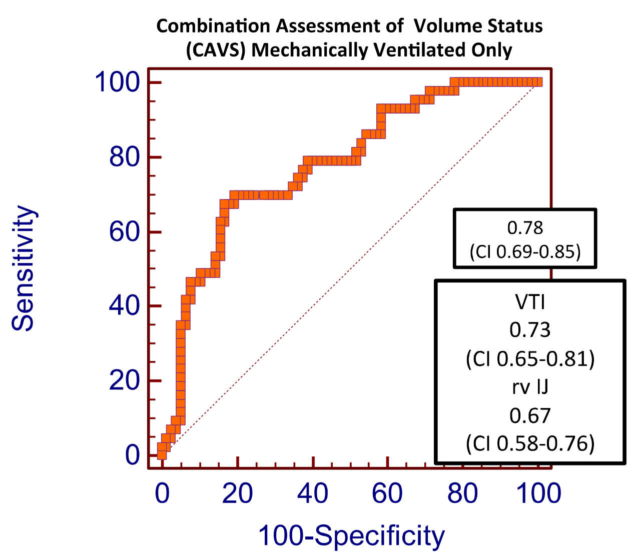

Figure 4. Combination assessment, VTI, and IJ in prediction of VR.

Table 3. Ranges of Predicative Variables

Parameter	-VR	_VR	% Measurable[a]	NPV/PPV (%)
CAVS	≤0.24	>0.40	73	70/80
VTI	≥22 cm/s	≤18 cm/s	78	74/70
0-90° IJ	≤12%	≥40%	75	61/64
rv IJ 90°	<12%	≥25%	79	71/60
rv SVV	<10%	≥15%	62	65/67
rv IVC	<10%	>50%	65	53/59

[a]% measurable is the percent of patients who were in either the upper or lower threshold categories.

5.4.2 Torso Surgery vs. No Torso Surgery. In the group as a whole, 46% had undergone thoracic or abdominal surgery. In patients with thoracic or abdominal surgery, VTI was most predicative, with an AUROC of 0.73, followed by RR IJ variation at 90 at 0.63. None of the other measures were predicative. In patients who did not have torso procedures, the accuracy was slightly less at 0.69 for VTI, but improved for IJ at 0.68. In this sub-group, SVV was predicative.

5.4.3 Summary of Sub-Group Analysis. Both mechanical ventilation and thoraco-abdominal surgery affect the accuracy of the US measurements. The measures are the most accurate in patients who are vented. The most accurate measures appear to be VTI and RR IJ variation at 90. When only vented patients are considered, the rSVV is also predicative. Other than VTI, none of the measures are likely to be predicative in patients who are not on the ventilator, although this was assessed in a small sub-group of 63 patients. Conversely, in mechanically vented patients, the measures are reasonably accurate, especially when considered together. Software tools could easily be developed to provide a useful non-invasive assessment of volume status in flight.

6.0 DISCUSSION

This study shows that US assessment of VR is a useful tool to guide fluid resuscitation; however, it is far from perfect. While cardiac function has been studied for decades by cardiologists, details about how to better manage fluid to perfuse end organs are particular to critical care and trauma management. Using US to predict the cardiac response to a fluid bolus is still new, and the details are developing.

Because it is a young field, the majority of ultrasound data has been collected in small homogenous groups of patients who are on the same mode of ventilation, receiving a certain type of bolus, very few of whom have had thoracic or abdominal surgery [19,24]. While this may yield an excellent AUROC, it is difficult to know how to apply these data in a more mixed, clinically relevant military population, on various modes of ventilation, and getting different types of fluid. Our data indicate that several US parameters are predicative of VR even in such a group. VTI, positional variation in the IJ, and respiratory variation in the IJ at 90° are all significantly associated with VR. However, the AUROC is only moderately predicative, with values from 0.65-0.73 when single measures are used. This is still far better than that observed with either clinical judgment or guided by a CVP, both of which are about 50% predicative [8,31]. Interestingly, combined assessment of VTI and rv IJ increased the AUROC to 0.76-0.78. It makes sense that assessing both RV inflow (IJ assessment) and LV outflow (VTI) will lead to a better method of assessment. CAVS holds promise and could likely be refined, but for common

use, software applications to assist in calculations would need to be developed. Hopefully, as the field of point-of-care US matures, these sorts of tools will come into fruition.

Of the two measures used for combined assessment, VTI is the most accurate. It is also the primary US determinant of SV and cardiac output. It is an established measure, routinely performed by most cardiology labs [30]. While VTI requires a more sophisticated system, the technique itself is not difficult. We have previously reported that it can be measured in >85% of surgical/trauma ICU patients, a finding this study confirms, as only 13% of patients were excluded because it could not be obtained. VTI assessment is already part of some point-of-care cardiac evaluations [28,29], and recently Blanco et al. proposed adding it to the rapid ultrasound in shock [32]. This study indicates that VTI may be the most important indicator of volume status, and consideration should be given to adding it to all critical care US exams. The currently available systems for use in flight are not able to asses VTI accurately.

Conversely, IJ assessment is easy to do with any US system, but how to perform it is less clear. In our study, respiratory variation at 90° appeared to be more predicative then positional change from 0-90°. Recently, Guarracino et al. also reported that rv IJ was predicative of VR. Guarracino used a different, and more complex, IJ assessment using M-mode to calculate cross-sectional area change [24]. This achieved an ROC of 0.92 in a small homogeneous population. It is possible that this is a superior method of IJ assessment, but it requires further validation in a larger and more heterogeneous population.

Of note, we did not observe an association between rv IVC and VR. The IVC is difficult to image in patients who have undergone abdominal surgery, and the yield was lowest for this metric at 78%. We also found that both the PPV and NPV were just above 50% for IVC, even when high and low end thresholds were used. This confirms data from other researchers showing that this measure is of questionable accuracy in critically ill patients [18-23]. Respiratory variation in the IVC still may have utility in some patients, especially during initial assessment in the Emergency Department prior to prolonged intubation and surgery.

Ultrasound is not a tool to be used like a laboratory blood test. There is literal grey area. Images may be sub-optimal (especially in trauma patients), and measurements are operator and experience dependent. Ejection fraction is described in large ranges because one can reliably tell <30% from over >55%, but differentiating between 41 and 46%, for example, is not reproducible. Physiologic US data are better understood as semi-quantitative, because they are inherently not precise. The major fields with experience in using US—vascular, radiology, and cardiology—use ranges and grading rather than specific single value cut-offs.

In distinction, most point-of-care US data report very specific values (rv IVC of 18 and 41% or 13% IJ change) for very specific populations—vented, not vented, spontaneous breathing, respectively—vs. a set rate [15,18,24]. This has created a pattern of multiple small studies published with excellent AUROCs that cannot be reproduced with follow-up testing. In small, tight data sets, with a limited number of operators (people performing the US), a single value is possible, but in larger, more true-to-life heterogeneous populations, ranges are likely to be the best way to understand US data—unlikely VR, possibly VR, more likely VR—rather than a binary yes/no. Using precise thresholds creates both a false sense of accuracy and non-reproducibility.

This study demonstrates that the ROC criterion can be used to identify upper and lower thresholds, creating ranges, which can be meaningfully evaluated in more heterogeneous data sets. The thresholds that arise from these data are similar to that published by others [12,24]. We detected rv SVV <10% and ≥15%. These values are very similar to those found with SVV using

pulse contour analysis [33,34]. Similarly, we report <12% for rv IJ and Guarracino reported 13% [24]. This lends credence to the argument that ranges may allow a more cohesive and accurate way to understand US as a semi-quantitative tool.

Ultrasound is an important tool in determining which patients will respond to fluid with an increase in SV. While US clearly can predict VR, the best measures are still being understood and validated. It appears that IJ and VTI assessments are likely to be the most accurate, especially when used together. Further research is warranted, as US is rapid, risk free, and relatively inexpensive. Our data in conjunction with that of others indicate that US for the assessment of VR is a helpful adjunct, but not quite ready for prime time in a critically ill surgical population.

7.0 CONCLUSIONS

In a relevant heterogeneous trauma population, US is predicative of VR, but it still needs to be refined and developed before widespread military use. These data suggest that upgrading the transport US machines should be considered, as VTI appears to be the most accurate predictor of VR and can be used to calculate SV and cardiac output. Internal jugular change and VTI are the best measures of VR, especially when used together. With the development of better software tools and upgrading the US systems, US could become an essential part of managing hemodynamically unstable patients during evacuation.

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LIST OF ABBREVIATIONS AND ACRONYMS

2D	two-dimensional
AP	apical
AUROC	area under the receiver operating characteristic curve
CAVS	combination assessment of volume status
CI	confidence interval
CVP	central venous pressure
FREE	focused rapid echocardiogram exam
ICU	intensive care unit
IJ	internal jugular
IVC	inferior vena cava
LV	left ventricle
M	mean
p∆IJ	positional internal jugular change
plr SVV	passive leg raise stroke volume variation
ROC	receiver operating characteristic curve
RR	respiratory rate
rSVV	respiratory stroke volume variation
rv	respiratory variation
RV	right ventricle
SD	standard deviation
SV	stroke volume
SVV	stroke volume variation
TTE	transthoracic echocardiogram
US	ultrasound
VR	volume response/responsiveness
VTI	velocity time integral